**Preparation of P proteins**

The cDNA encoding the P domain of the epidemic strain was cloned into the vector pGEX-4T-1 (Amersham Biosciences, Piscataway, NJ) between Bam HI and Not I sites for protein expression. After sequence confirmation, P proteins were expressed in E. coli as described previously[[1](#_ENREF_1)]. Briefly, the BL21 culture was induced by IPTG (isopropyl-β-D-thiogalactopyranoside) at a concentration of 0.5 mM at 22°C overnight. The recombinant P-GST fusion protein was purified using Glutathione Sepharose 4 Fast Flow resin (GE Healthcare Life Sciences, NJ, USA). The GST was then removed by thrombin (GE Healthcare Life Sciences, NJ, USA) cleavage on beads at 22°C overnight[[2](#_ENREF_2)].

**Analysis of HBGA-binding interfaces and the surrounding region of GII.6 clusters**

Ten representative strains were selected from GII.6 cluster a-c to compare with the sequence of the epidemic strain. The P domain sequences were aligned and analyzed, focusing on the HBGA-binding interfaces and the surrounding regions. The alignment with reference strains was performed using the MegAlign program in DNAstar 7.1.

(1) **Tan M, Hegde RS, Jiang X.** The P domain of norovirus capsid protein forms dimer and binds to histo-blood group antigen receptors. *Journal of virology* 2004; **78**(12): 6233-6242.

(2) **Zhang XF, et al.** An outbreak caused by GII.17 norovirus with a wide spectrum of HBGA-associated susceptibility. *Scientific reports* 2015; **5**: 17687.